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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,892	03/09/2004	Han-Chung Wu	P/741-177	2636

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,892	WU ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

The Election filed on 3/13/2006 in response to the Restriction Requirement of 2/23/2006 has been entered. Applicant's election of Group I, claims 1-12, as specifically drawn to a peptide marker has been acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The restriction requirement is therefore deemed to be proper and is made FINAL.

Claims 1-16 are currently pending

Claims 13-16 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-12 are currently under consideration.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

Figure 4 A-H are objected to under 37 CFR 1.83(a) because they fail to show the immunofluorescence staining of L-peptide-liposome-HPTS complex on NPC cells as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not

accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

The specification on page 8, paragraph 0026 describes parts A-D of Figure 4, but appears to be silent on E-L.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 5-7, as written, do not sufficiently distinguish over peptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 4, paragraph 0012 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5, 7-8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Longmuir et al. (US 6,372,720, 2002).

Longmuir et al. teach a liposome complex comprising a non-cationic lipid, a fusogenic peptide and a substance to be delivered to a cell and/or nucleus (abstract). With regards to the fusogenic protein, the patent teaches (column 3, lines 27-49) a peptide which comprises the instantly claimed peptide of SEQ ID NO: 2. Moreover, Longmuir et al. teaches that the liposomal complex's can be used to treat tumors which require delivery of a substance intracellularly and/or intranuclearly (column 9, lines 8-15). Thus, while Longmuir et al. does not explicitly teach that the peptide specifically binds to nasopharyngeal carcinoma which can lead a liposome to NPC cells, the claims are drawn to the product *per se* and inherently, such a polypeptide comprising the claimed amino acid sequence of SEQ ID NO: 2 would bind and lead a liposome to NPC cells. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Moreover, although Longmuir et al. do not explicitly teach that the peptide can be applied as a detector in the development of NPC cell diagnostic kit, the intended use of the compound, i.e development of a NPC cell diagnostic kit, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Claims 1-3, 5-8 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Sette et al. (WO 01/00225 A1, 2001) as evidenced by Kunisawa et al. (J. Controlled Release 2005; 105: 344-353).

Sette et al. teach a peptide comprising the instantly claimed peptide of SEQ ID NO: 2 (page 53, Table 9, peptide 1404.22 of the WO document). Moreover, the reference teaches that the

peptide can be administered via a liposome, wherein the peptide is incorporated into the liposome along with another therapeutic molecule (page 34, lines 7-10). Sette et al. further teach that the peptides can be administered to a mammal for the treatment of cancer (page 25, lines 23-25). Thus, while Sette et al. does not explicitly teach that the peptide specifically binds to nasopharyngeal carcinoma which can lead a liposome to NPC cells, the claims are drawn to the product *per se* and inherently, such a polypeptide comprising the claimed amino acid sequence of SEQ ID NO: 2 would bind and lead a liposome to NPC cells. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Moreover, although Sette et al. do not explicitly teach that the peptide can be applied as a detector in the development of NPC cell diagnostic kit, the intended use of the compound, i.e development of a NPC cell diagnostic kit, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982). Lastly, even though Sette et al. do not explicitly teach that the liposome enters the cell though endocytosis, the claimed functional limitation would be an inherent property of the referenced liposome because as evidenced by Kunizawa et al, conventional liposomes encapsulated with nanoparticles results in an endocytosis-mediated cellular uptake of the nanoparticle (abstract). Hence, even though the claims are drawn to a mechanism by which the liposome is incorporated into a cell, the claimed product does not appear to distinguish over the prior art teaching of the same or nearly the same product. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or

obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3-5 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martin et al. (2002/0172711 A1, 2002) in view of Longmuir et al. (US 6,372,720, 2002).

Martin et al. teach a fusogenic liposome composition for delivering a liposome-entrapped compound into the cytoplasm of a target cell (abstract). With regards the entrapped compound, the publication teaches that the encapsulated drug includes, but is not limited to, doxorubicin (page 11, paragraph 140).

Martin et al. do not explicitly teach that the fusogenic peptide comprises SEQ ID NO: 2.

Longmuir et al. teach a liposome complex comprising a non-cationic lipid, a fusogenic peptide and a substance to be delivered to a cell and/or nucleus (abstract). With regards to the fusogenic protein, the patent teaches (column 3, lines 27-57) that the fusogenic peptide includes, but is not limited to, a peptide which comprises the instantly claimed peptide of SEQ ID NO: 2, wherein the peptide facilitates the transfer of the liposomes complex and its contents across the cell membrane. Moreover, Longmuir et al. teaches that the liposomal complex's can be used to treat

tumors which require delivery of a substance intracellularly and/or intranuclearly (column 9, lines 8-15).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to incorporate the fusogenic peptide comprising the amino acid sequence of SEQ ID NO: 2 in the liposome composition encapsulated with doxorubicin taught by Martin et al. in view of the teachings of Longmuir et al. that the peptide comprising SEQ ID NO: 2 facilitates the transfer of the liposomal complex and its contents across the cell membrane. One would have been motivated to do so because Longmuir et al. teaches that the liposomal complexes comprising the fusogenic peptide comprising SEQ ID NO: 2 can be used to treat tumors which require intracellular delivery or intranuclear delivery of the substance into the tumor. Thus, one of ordinary skill in the art would have a reasonable expectation that by incorporating the fusogenic peptide comprising the amino acid of SEQ ID NO: 2 in to the liposome composition as taught by Martin et al., one would achieve an effective liposomal complex for intracellular delivery of doxorubicin.

Claims 3-5 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sette et al. (WO 01/00225 A1, 2001) as evidenced by Kunisawa et al. (J. Controlled Release 2005; 105: 344-353) in view of Vaage et al. (Cancer; 1994: 73; 1478-1484).

Sette et al. teach, as applied to claims 1-3, 5-8 and 11-12 above, a peptide comprising the instantly claimed peptide of SEQ ID NO: 2 (page 53, Table 9, peptide 1404.22 of the WO document). Moreover, the reference teaches that the peptide can be administered via a liposome, wherein the peptide is incorporated into the liposome along with another therapeutic molecule (page 34, lines 7-10). Sette et al. further teach that the peptides can be administered to a mammal for the treatment of cancer (page 25, lines 23-25).

Sette et al. do not explicitly teach that the liposome further comprises a chemotherapeutic such as doxorubicin.

Vaage et al. teach the tissue distribution and therapeutic effect of intravenous free or encapsulated liposomal doxorubicin on human prostate carcinoma xenografts (title). Specifically, the reference teaches that the liposomal formulation resulted in a 25-fold increase in doxorubicin at the disease site and was more effective than the free drug in inhibiting growth.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to generate a chemotherapeutic drug comprising a peptide comprising the amino acid sequence of SEQ ID NO: 2 as taught by Sette et al. and doxorubicin as taught by Vaage et al. encapsulated in a liposome because each of the liposomal complexes have been individually taught in the prior art to be successful at cancer. The instant situation is amenable to the type of analysis set forth in In re Kerkhoven,205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, one of ordinary skill in the art would have reasonable expectation of success that by encapsulating a peptide comprising the amino acid sequence of SEQ ID NO: 2 as taught by Sette et al. and doxorubicin as taught by Vaage et al. into a liposome, one would achieve a chemotherapeutic agent effective for the treatment of cancer.

Conclusion

No claim is allowed.

Skeiky et al. (WO 01/81581 A2, 2001, only relevant pages), whom is considered the closest prior art to a peptide comprising the amino acid sequence of SEQ ID NO: 1, teach a peptide having 63.6% identity to the instantly claimed peptide comprising the amino acid sequence of SEQ ID NO: 1 (see below). However, Skeiky et al. do not teach or suggest a peptide comprising the amino acid sequence of SEQ ID NO: 1. Therefore, the peptide comprising the amino acid sequence of SEQ ID NO: 1 appears to be free of the prior art.

```
PN   WO200181581-A2.
PD   01-NOV-2001.
PI   Skeiky YAW,  Persing DH,  Mitcham JL,  Wang SS,  Bhatia A;
PI   L'maisonneuve J,  Zhang Y,  Jen S,  Carter D;
SQ   Sequence 117 AA;
```

Example 1; SEQ ID NO 23289; 1069pp

```
  Query Match             64.1%;  Score 41;  DB 4;  Length 117;
  Best Local Similarity   63.6%;  Pred. No. 32;
  Matches    7;  Conservative    3;  Mismatches    1;  Indels    0;  Gaps
0;
```

```
Qy          1 RLLDTNRPLLP 11
              |||:| ||::|
Db         80 RLLETRRPVVP 90
```

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER